REVIEW

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Dysbiosis in Multiple Sclerosis: Can Immunoglobulin Y Supplements Help?

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ABSTRACT

The role of gut microbiota in autoimmune disorders like multiple sclerosis is gaining attention. Multiple sclerosis is characterized by inflammation, demyelination, and neurodegeneration in the central nervous system. Alterations in gut microbiota have been linked to multiple sclerosis development, with decreased beneficial bacteria and increased harmful species. The gut-brain axis is a complex interface influencing bidirectional interactions between the gut and the brain. Dysbiosis, an imbalance in gut microbiota, has been associated with autoimmune diseases. The influence of gut microbiota in multiple sclerosis is reversible, making it a potential therapeutic target. Probiotics, prebiotics, and fecal microbiota transplantation have shown promise in multiple sclerosis treatment, with positive effects on inflammation and immune regulation. Immunoglobulin Y (IgY) supplements derived from chicken egg yolk have potential as nutraceuticals or dietary supplements. IgY technology has been effective against various infections, and studies have highlighted its role in modulating gut microbiota and immune responses. Clinical trials using IgY supplements in multiple sclerosis are limited but have shown positive outcomes, including reduced symptoms, and altered immune responses. Future research directions involve understanding the mechanisms of IgY's interaction with gut microbiota, optimal dosage determination, and long-term safety assessments. Combining IgY therapy with other interventions and investigating correlations between microbiota changes and clinical outcomes are potential avenues for advancing multiple sclerosis treatment with IgY supplements.

Key words: multiple sclerosis – gut microbiota – dysbiosis – probiotics – immunoglobulin Y.

Abbreviations: CNS: central nervous system; EAE: autoimmune encephalomyelitis; Ig: immunoglobulin; MS: multiple sclerosis; PPMS: primary progressive MS; PRMS: progressive-re-lapsing MS; SPMS: secondary progressive MS; RRMS: relapsing-remitting MS; SCFA: short-chain fatty acids; TGF: tumor growth factor; Th: T helper; TLR: Toll-like receptors; Treg: T regulatory cells.

INTRODUCTION

Multiple sclerosis (MS) is a chronic autoimmune neurological disorder characterized by inflammation, demyelination and neurodegeneration in the central nervous system that results in a multitude of symptoms including vision loss, motor deficits, bowel dysfunction, depression, and cognitive impairment due to immune reactions against myelin proteins and gangliosides. Multiple sclerosis is primarily divided into progressive-re-lapsing MS (PRMS), primary progressive MS (PPMS), secondary progressive MS (SPMS), relapsing-remitting MS (RRMS) [1]. There are several factors which are considered responsible for the initiation of MS, which includes intestinal dysbiosis, vitamin D deficiency, a hypercaloric diet, and viral infections, but major factors responsible for triggering MS are genetic and environmental factors [2]. In recent years, there has been growing interest in the role of the gut microbiota in the development and progression of MS. Studies have shown that individuals with MS have alterations in their gut microbiota composition, including a decrease in the abundance of certain beneficial bacteria mainly belonging to *Firmicutes* or *Bacteroidetes* genera and in the presence of the short-chain fatty acids (SCFA) producing bacteria strains, and an increase in potentially harmful bacteria including *Akkermansia muciniphila*. These changes may contribute to the development of MS by promoting inflammation and immune dysregulation [3].

Research has also shown that the gut microbiota may play a role in modulating the effectiveness of MS treatments. This suggests that interventions that target the gut microbiota, such as probiotics, immunoglobulin Y supplements, fecal microbiota transplantation, could potentially be used as adjuvant therapies for MS [4]. However, it is important to note that the exact mechanisms by which the gut microbiota influences MS are not yet fully understood, and further research is needed to determine the causal relationship between gut microbiota alterations and MS development and progression.

Immunoglobulin Y (IgY) is a type of antibody that is derived from chicken egg yolk and has been investigated for its potential therapeutic benefits in a variety of conditions: infectious disease, dental caries, periodontitis and autoimmune diseases.

This review aims to provide an overview of the current understanding of the role of the gut microbiota in MS pathogenesis, to evaluate the potential of IgY supplementation in modulating the gut microbiota, to identify the gaps in current knowledge and highlight the directions for future research on the use of IgY supplementation in MS treatment.

GUT MICROBIOTA AND IMMUNE SYSTEM

The human gut microbiota, consisting of over 100 trillion microorganisms from 500 bacterial genera, plays a crucial role in directing both pro- and anti-inflammatory immune responses [5, 6]. This interplay is influenced by factors such as gut microbial structure, host genetics, age, and gender. Gut microbiota is recognized as a potential target for diagnosis, prognosis, and therapeutic interventions in autoimmune disorders. Recent research underscores the microbiome‘s essential role in shaping host immune responses and its impact on susceptibility to immune-mediated and infectious diseases [5, 7, 8]. The intestinal immune system, critical for maintaining immune tolerance, supports harmless microorganisms‘ proliferation while generating responses against pathogens [7, 9, 10].

The Interplay between Gut Microbiota and Innate Immunity

The relationship between innate immunity and gut microbiota is bidirectional. Antimicrobial peptides produced by intestinal microbiota are crucial for maintaining immune homeostasis [11]. Toll-like receptors (TLR) serve as pattern recognition receptors, defending against pathogens and regulating commensal microorganisms [12]. Commensal microbe *Bacteroides fragilis* promotes symbiosis and host immunity. Murine models show an altered microbial composition in MyD88-deficient mice, impacting microbial homeostasis and T-cell differentiation. Gut microbiota produces NOD ligand metabolites, influencing intestinal immune cells and promoting microbial homeostasis. Foxp3+ T regulatory cells (Treg) cells and Tfh/ex-Th17 cells contribute to commensal microbiota compartmentalization [13, 14].

The Interplay between Gut Microbiota and Adaptive Immunity

The adaptive immune system is significantly influenced by interactions between host and microbiota [15]. B cells producing IgA antibodies play a vital role in maintaining gut homeostasis. T-cell dependent production of IgA shapes gut microbial communities and maintains a balanced and diversified microbiome, supporting the expansion of Foxp3+ Treg cells [16–18]. The lack of bacterial strains fermenting dietary fiber into SCFAs results in the absence of intestinal CD4+ Treg cell differentiation [19, 20]. T helper (Th) 17 cells produced by segmented filamentous bacteria and Tfh cells contribute to maintaining microbial homeostasis [21]. Emerging studies highlight the influence of tissue resident DCs on intestinal microbiota, revealing the crucial role of Syk kinase-coupled signaling pathways and NF-κB-inducing kinase in microbiota-induced immune responses [22].

GUT-BRAIN AXIS

The gut-brain axis is a complex interface involving bidirectional pathways such as immune regulation, intestinal barrier maintenance, and gut endocrine signaling. The central nervous system (CNS) influences gut function through dense innervation and local immune responses. Recent studies highlight the crucial role of the gut microbiota in bidirectional communication between the gut and the brain, impacting central nervous system functions. Communication occurs through neural, metabolic, endocrine, and immunological pathways [23].

MECHANISM UNDERLYING DYSBIOSIS IN AUTOIMMUNE DISEASES

The imbalance in the microbiota is termed as “dysbiosis.” Alterations in the gut microbial composition have been associated with disturbed gut barrier functions, enhanced gut permeability, and increased plasma lipopolysaccharide concentrations, which results in inflammation that predisposes the host for obesity, metabolic syndrome, and autoimmune diseases [24, 25]. The leaky gut leads to the liver autoimmune reactions because the mucosal lymphocytes migrate to the liver through the altered gut barrier [26].

Dysbiosis can also promote autoimmunity by several key mechanisms such as molecular mimicry wherein autoimmune reactions can be triggered by gut microbiota by providing cross-reactive antigens to T cells [27-29]. One study proved the ability of commensal bacteria to mimic several autoimmune immunogens and the role this plays in the pathogenesis of MS [30]. Moreover, the bystander activation of antigen-presenting cells leading to proinflammatory cytokine production is considered a possible mechanism in the development of autoimmunity [28]. The evidence provided suggests the role of dysbiosis in promoting and exacerbating autoimmune disorders. However, the influence on the immune system of gut microbiota is reversible and therapeutic manipulation of the microbiome can restore proper immune function.

Microbiota Changes and Dysbiosis in Multiple Sclerosis

A high prevalence of “leaky gut” and alterations of gut microbiota have been found in experimental autoimmune encephalomyelitis (EAE) animals and in MS patients [31]. An increased proinflammatory cell infiltration and impaired Treg function are immunological changes that characterize

EAE. The favorable gut microbiota can activate microglia, limit astrocyte pathogenicity, and regulate permeability of blood brain barrier [22, 32]. The presence of bacteria strains like *Clostridium*, *Bacteroidetes*, *Prevotella*, *Parabacteroides* and *Lactobacillus* in gut microbiota can induce production of SCFAs [33, 34] and helps in the maintenance of immune cells which produces anti-inflammatory response [35, 36]. The EAE symptoms severity is reduced by lactic acid-producing bacteria such as *Lactobacillus* and by the *Bifidobacterium*. On the other hand, when stools from individuals with MS were transplanted into the gut of mice with induced or spontaneous autoimmune encephalomyelitis the neurological symptoms worsen, thus supporting the association of the pro-inflammatory gut microbiota and MS [37-39].

Relapsing-remitting MS is characterized by a higher relative abundance of bacteria responsible for pro-inflammatory reactions produced by CD4+ T cells dendritic cells, monocytes or B cells [36] and lower relative abundance of bacteria responsible for producing anti-inflammatory responses by immune cells such as Tregs, CD4+ T cells which produces interleukin (IL)-10, regulatory B cells, suppressive macrophages and tolerogenic dendritic cells.

In MS patients, *Firmicutes* and *Bacteroidetes* phyla are lower or even depleted and the abundance of *Archae* is high. The *Bacteroides* and *Clostridia* species are especially responsible for the induction of Foxp3+ Tregs in suppression of inflammation. As one small longitudinal study highlighted, some gut microbiota profiles, especially *Fusobacteria*, are associated with increased risk of relapses [40]. *Parabacteroides*, *Prevotella* and *Adlercreutzia* genera were detected to be much lower in MS patients, while *Haemophilus*, *Blautia*, *Dorea* and *Pseudomonas* genera were increased. Clostridiales including *Faecalibacterium*, *Ruminococcus*, *Lactobacillaceae*, *Bacteroidaceae* and *Clostridium* were restored after MS treatment with glatiramer acetate [41]. The recent literature reviewed on the composition of the MS gut microbiota is mentioned in Table I [31, 37, 40, 42-46]; the changes in gut microbiota are associated with MS development, but a clearer understanding of the role of the gut microbiome in MS is crucial in developing targeted therapeutics.

The role of Probiotics in Treating Dysbiosis in Multiple Sclerosis

A few animal and human studies have already validated the beneficial role of fecal microbial transplantation, probiotic and prebiotic treatment in MS [48, 49]. A study on probiotic *Escherichia coli* Nissler 1917 in EAE mice model showed a decrease in the susceptibility of neuroinflammation [50] by lower values of inflammatory cytokines: IL-17, IFN-γ, TNF-α and higher values of IL-10, autoreactive CD41 T cells and CD41FOXP31 cells in lymph nodes. In another study, treatment with IRT5 (mixture of five probiotics containing of 108 CFU/g of each strain: *Streptococcus thermophilus*, *Lactobacillus acidophilus*, *Lactobacillus casei*, *Bifidobacterium bifidum* and *Lactobacillus reuteri*) contributed to the suppression of the EAE condition [51]. The combination of *Lactobacillus plantarum* DSM 15312, *Lactobacillus plantarum* DSM 15312, and *Lactobacillus paracasei* DSM 13434 also showed therapeutic potential in inhibiting the progression of myelin oligodendrocyte glycoprotein induced EAE [52]. The probiotic combination of *Bifidobacterium animalis* and *Lactobacillus plantarum* A7 is able to improve EAE condition bt increasing Treg cells with an increased expression of CD251, CD41, and Foxp31 in lymph nodes and spleen along with Th2 cells and antiinflammatory cytokines levels [such as IL-4, tumor grows factor (TGF-β), and IL-10]. At the same time, a subsequent decrease in IL-6 and IL-17 cytokines and Th17 and Th1 cells was observed, resulting in a decrease in inflammation,

Table I. Key findings on MS gut microbiota in scientific literature. MS cases versus controls

Author, Year of Publication, Reference	Study design	Biological sample	Key findings in MS cases
Mowry, 2012 [42]	Case-control	stool	Lower relative abundance of *Faecalibacterium* RRMS cases
Rumah, 2013 [43]	Case-control	stool	Human gut colonization by *Clostridium perfringens* type B in an MS patient
Cantarel, 2015 [44]	Case-control, intervention, pilot study	stool	Lower relative abundance of *Faecalibacterium*
Miyake, 2015 [45]	Case-control	stool	Lower relative abundance of *Prevotella copri* and *Clostridium* in RRMS cases Higher relative abundance of *Bilophila wadsworthia* in MS
Chen, 2016 [31]	Case-control	stool	Higher relative abundance of *Dorea* and *Blautia* Lower relative abundance of *Adlercreutzia equolifaciens* and *Collinsella* Higher abundance of *Mycoplana* and *Pseudomonas*
Tremlett,2016 [40]	Case-control, pilot study	stool	Increased colonization of *Firmicutes* in pediatric MS patients
Jangi, 2016 [46]	Case-control	stool	Lower relative abundance of *Sutterella*, *Collinsella* and *Slackia*
Cekanaviciute, 2017 [38]	Case-control	stool	Lower relative abundance of *Parabacteriodes distasonis; Acinetobacter calcoaceticus* stimulates pro-inflammatory Th1 cytokines, aggravating MS Akkermansia muciniphila may enhance the production of proinflammatory cytokines
Swidsinki, 2017 [47]	Case-control, intervention	stool	Lower relative abundance of *Faecalibacterium prausnitzii*
Berer, 2017 [37]	Case-control, co-twin	stool	Higher relative abundance of *Akkermansia muciniphila*

MS: multiple sclerosis; RRMS: relapsing-remitting MS.

autoreactive T cells, and demyelination [53]. Moreover, as an effect of probiotic administration, SCFAs are produced, such as acetate, propionate, and butyrate. These SCFAs along with TLRs maintain immune homeostasis. It results in elevated levels of IL-10 and TGF-β cytokines, which further enhance Treg production and contribute to immune regulation, leading to reduced demyelination in CNS of MS patients.

Recent human studies have assessed significant remission of clinical aspects and positive metabolic response when administering probiotics in MS patients. The B cells' function was observed to rapidly decline after 12 weeks of probiotics capsule administration containing probiotics strains of *Lactobacillus casei*, *Bifidobacterium bifidum*, *Lactobacillus fermentum*, and *Lactobacillus acidophilus*. This randomized, placebo-controlled clinical trial on probiotics capsules conducted on 60 MS patients suggested that the uptake of this probiotic improved depression, anxiety and stress scales of the patients. Moreover, the levels of nitric oxide, CRP and malondialdehyde were significantly altered within the placebo group [54].

A randomized, double-blind, placebo-controlled clinical trial enrolled 40 MS patients and randomly divided them into two groups, where one group received a probiotics capsule containing *Lactobacillus fermentum*, *Bifidobacterium bifidum*, *Lactobacillus acidophilus*, and *Lactobacillus casei* with $23x10^9$ CFU/g each and the other group was assigned to receive a placebo for 12 weeks. The aim was to evaluate the role of probiotics on the genetic expression related to glucose, lipid, and inflammatory pathways and they reported a downregulation of TNF alfa and IL8 mRNA expressions in the peripheral blood mononuclear cells of MS patients as a result [55].

The human studies that we reviewed [54-57] (Table II) demonstrated that probiotic administration had a positive impact on the progression and delay in the onset of the disease, suggesting that probiotics have immunomodulatory effects in MS patients.

RATIONALE FOR USING IMMUNOGLOBULIN Y SUPPLEMENTS

Immunoglobulin (Ig) Ys are produced by chickens and other birds, reptiles, and amphibians. Among avian IgY, chicken IgY has been the most studied and characterized. IgYs are present in the sera of chickens and are passed to the embryo through the egg yolk. The function of IgYs is similar to that of mammalian IgGs. Although functional similarity exists between IgY and IgG, their structures are quite different.

Table II. Major findings in human studies of probiotic therapies in MS

Study, Year of publication	Intervention	Duration	Major Findings	
			Clinical	Immuno-metabolic
Kouchaki, 2017 [54]	I: Probiotic capsule 2*109 CFU • *Lactobacillus. acidophilus* • *Lactobacillus casei* • *Lactobacillus fermentum* •*Bifidobacterium bifidum* C: Starch capsule	2x a week For 12 weeks	EDSS ↓ BDI ↓ DASS ↓ GHQ-28 ↓ Probiotic capsule improves depression, anxiety, and stress scale within the patients	Hs-CRP ↓ MDA ↓ Plasma NO ↑ The levels of CRP, malondialdehyde, and plasma nitric oxide were significantly changed within the placebo group
Rahimlou, 2020 [56]	I: Protexin capsule 2*109 CFU C: Maltodextrin capsule	1x a day For 6 months	EDSS – BDI ↓ GHQ-28 ↓ FSS ↓ MPQ ↓	IL-6 ↓ BDNF ↑ NGF -
Salami, 2019 [57]	I: Probiotic capsule 2*109 CFU • *Lactobacillus plantarum* • *Lactobacillus casei* • *Lactobacillus fermentum* • *Lactobacillus reuteri* • *Bifidobacterium lactis* • *Bifidobacterium infantis* C: Maltodextrin capsule	Unknown frequency For 16 weeks	EDSS ↓ BDI – DASS ↓ GHQ-28 –	Hs-CRP ↓ MDA ↓ 8-OHdG ↓ IL-10 ↑ TAC ↑ GSH ↑ NO ↑ IL-6 ↓ TNF-α ↓
Tamtaji, 2017 [55]	I: Probiotic capsule 2*109 CFU • *Lactobacillus acidophilus* • *Lactobacillus casei* • *Lactobacillus fermentum* • *Bifidobacterium bifidum* C: Starch capsule	1x a day For 12 weeks	BMI – No relapse –	IL-1 – TNF-α↓ IL-8 ↓ Downregulation among the gene expression of TNF-α mRNA and IL-8 in the peripheral blood mononuclear cells of MS patients. Probiotics has a modulating effect in the inflammatory cytokines of MS patients

8-OHdG: 8-Oxo-2'-deoxyguanosine; BDI: Beck Depression Inventory; BDNF: brain-derived neurotrophic factor; CFU: colony-forming unit; DASS: Depression Anxiety Stress Scales; EDSS: Expanded Disability Status Scale; FSS: Fatigue Severity Scale; GHQ-28: General Health Questionnaire-28; GSH: glutathione; hs-CRP: high-sensitivity C-reactive protein; IL: interleukin; McGill Pain Questionnaire; MDA: malondialdehyde; mRNA: messenger ribonucleic acid; MPQ: NGF: nerve growth factor; NO: nitric oxide; TAC: total antioxidant capacity; TNF-α: tumor necrosis factor.

Among the differences, the H chain of IgYs have one variable region (VH) and four constant regions (CH) regions, while mammalian IgGs have only three CH regions. Also, IgY lacks a hinge region between the CH1 and CH2 domains, making it less flexible than IgG. Compared with mammalian IgG, chicken IgY has 3 to 5 times more affinity and reacts more rapidly to the same antigens when tested in competition assays. IgY antibodies are obtained by immunizing the hen with the antigen of interest. A small amount of antigen in the milligram or microgram range usually elicits enough IgY response and the antibody titers persist over several weeks to several months [58].

IgY itself is not a probiotic or prebiotic as it does not contain live microorganisms or complex carbohydrates that can selectively stimulate the growth of beneficial gut bacteria, but it can be considered a nutraceutical or a food supplement. Polyclonal IgY antibodies have been present in the market for more than two decades in different products such as Ig-Guard Mutant and Ovalgen® DC (*Streptococcus mutans*), Ovalgen® PG (*Porphyromonas gingivalis*), and Ovalgen® CA (*Candida albicans*) recommended for oral cavity infections; Ovalgen® FL for influenza; anti-SARS-CoV-2 IgY; Ig-Guard Helico, GastimunHP, Ovalgen® HP (*Helicobacter pylori*), Ig-Guard Rota, Ovalgen® RV (Rotavirus) for gastrointestinal diseases; IgY Max (against 26 human-relevant bacteria); Imunoinstant G® (against 30 pathogens) used also as an adjuvant treatment for psoriasis and other autoimmune conditions. In contrast to the typical perception of antibody products, IgY is designated as GRAS (generally recognized as safe) by the US Food and Drug Administration (FDA). Regulations governing the licensing of IgY products are relatively lenient, particularly for applications such as food supplements or oral use. Nevertheless, strict regulations are in place for products intended for parenteral administration and monoclonal IgY. Taking into consideration that modulating gut microbiota is the main objective in dysbiosis, the oral administration of polyclonal IgY along with encapsulation materials and stabilizers can be achieved using egg yolk powder containing specific IgY as the most economical and practical dosage form [59].

Immunoglobulin Y therapy has several attractive characteristics including lack of reactivity with the human complement system and human Fc-receptors, thereby preventing non-specific inflammation. Because IgY does not react with the human complement system or Fc receptors, the risk of further inflammation is minimal. Egg allergies usually involve egg albumin components which may explain why no reactivity issues have been encountered in consumer use of several products now available on the market containing purified IgY. Immunoglobulin Y is thought to work by binding to the bacteria or viruses, leading to their elimination through the gut therefore leading to prevention of bacterial replication or virus spread. In some cases, passive immunization using IgY antibodies has rapid and local onset of action and can be given to patients with active infection. It can also be used in immature or impaired immune response, such as infants and immuno-compromised adults. Immunoglobulin Y is an effective immunologic tool to fight infection, involving microbes colonizing the alimentary tract of humans. It is relatively safe being found in the daily human diet, and can exert its activity within the entire length of the alimentary tract in predictable manner [60]. Regarding systemic administration, further safety studies are required, despite the lack of cross-reactivity between IgY and mammalian Fc. These safety concerns can be reduced also by developing the chimeric antibody fragments and humanized monoclonal IgY [59].

Clinical Applications of Immunoglobulin Y Supplements

In the last years, an increasing number of studies have focused on the use of IgY in the treatment and prevention of infectious diseases in a variety of animal species and on their role of a nutraceutic in human medicine. It has been established that oral administration of antimicrobial immunoglobulins derived from bovine milk and poultry egg is an effective way to provide protective immunity against a variety of viral or bacterial pathogens which might reduce

The clinical use of antibiotics and thereby minimize the risk of bacteria developing antibiotic resistance as well as the risk of imbalance in commensal gut microbiota [60].

Oral administration of IgY has been successfully used to prevent or treat specific diseases including infant rotavirus diarrhea [60], *Helicobacter pylori* infection [61], dental caries (*Streptococcus mutans*) [62], periodontitis (*Porphyromonas gingivalis*) [63] and oral candidiasis (*Candida albicans*) [64]. With a mechanism of action that depends on direct intermolecular contact, specific IgY has been shown to reduce bacterial or viral load and their accompanying symptoms. A randomized, controlled trial conducted on 150 children with *rotavirus* enteritis compared the therapeutic effect of probiotics and oral immunoglobulin. The study population was randomly divided into control, probiotic and immunoglobulin groups and they received either a placebo, live combined *Bifidobacterium* and *Lactobacillus* tablets, or orally given anti-rotavirus egg yolk IgY. While both groups who received treatment had reduced intestinal flora imbalance, the group that took anti-rotavirus egg yolk IgY had a shortened course of the disease, and the elimination of the rotavirus was faster [65].

Immunoglobulin Y technology can be used in the prophylaxis of celiac disease, as one study demonstrated by developing a powdered egg yolk formula with protective sugars containing anti-gliadin IgY that retained its activity in vitro after being submitted to chemical conditions similar to those of the stomach and small intestine. This formula neutralized in vitro not only the isolated gliadin, but also that present in the food matrix and inhibited its intestinal absorption in mice [66].

In cystic fibrosis, mucus in the lungs leads to respiratory infections with *Staphylococcus aureus*, *Haemophilus influenzae*, *Burkholderia cepacia* and *Pseudomonas aeruginosa*, which are the main ones causes of lung tissue destruction, lung failure and death. Immunotherapy with specific IgY is an alternative to antibiotics used in prevention of pulmonary infections with *Pseudomonas aeruginosa* and could be a potential means of prevention of respiratory tract infections and treatment of some of them such as tuberculosis, infections secondary diseases associated with immunodeficiencies and infections with human immunodeficiency virus, common colds [67].

It is also important to mention that IgY technology has proved antifungal and antiparasitic activity. By using anti-lipase

IgY, the hydrolysis of diet fat can be inhibited, and its intestinal absorption can be reduced, therefore IgY technology can be used in treatment of obesity. IgY technology has an antitumor activity by producing IgY against tumor antigens which can represent an alternative for a more selective treatment of cancers and its use could; therefore, minimize the side effects of traditional chemotherapy.

Immunoglobulin Y Supplements in Dysbiosis and Multiple Sclerosis – Future Directions

With the increasing evidence connecting multiple sclerosis to the altered gut microbiota, there is a quest for chemicals that positively influence its composition and activity through dietary intake.

Immunoglobulin gY is, from a technical point of view, a nutraceutical or a food supplement. Being extracted from chicken egg, IgY supplements also contain ovotransferrin, lysozyme, ovomucin, other bactericidal proteins and complex immunomodulator proteins complex immunomodulator (transfer molecules and specific radicals). Furthermore, IgY may have potential as a postbiotic modulator, as it has been shown to have immunomodulatory effects in the gut and may interact with the gut microbiota to support their growth and activity, shaping through this interaction its composition and diversity. More research is needed to fully understand the potential role of IgY in the gut microbiota, and to elucidate the specific mechanisms by which IgY interacts with the inflammatory cytokines and gut microbiota and modulates its composition and activity by studying the molecular pathways and signaling involved in this interaction.

There is currently a lack of clinical trials designed to assess the efficacy and safety of IgY supplements administration in individuals with multiple sclerosis and associated gut dysbiosis. These trials should include study designs, appropriate control groups and outcome measures that evaluate both gut microbiota changes and clinical parameters in MS patients. Determining the optimal dosage and duration of IgY supplements administration in order to achieve maximum benefits in terms of modulating the gut microbiota and improving MS symptoms is another key aspect that needs to be established and this could involve conducting dose-ranging studies and long-term follow-ups of the sustained effects of IgY supplements.

Other future directions could be exploring the potential synergistic effects of combining IgY therapy with other interventions, such as specific probiotic, prebiotics, or dietary modifications, to optimize gut microbiota and investigating the potential links between IgY-induced changes in the gut microbiota and clinical outcomes in multiple sclerosis. How microbiota profiles correlate with disease progression, disability measures, and other relevant clinical markers will help to better understand the therapeutic implications of IgY supplements administration.

Long-term follow-up studies can provide valuable insight into the durability of microbiota changes and any potential adverse effects associated with prolonged IgY supplementation by assessing the long-term effects and safety profile of IgY supplements administration, including potential interactions with medications commonly used in multiple sclerosis treatment.

CONCLUSIONS

Dysbiosis have been linked to MS development. The influence of gut microbiota in MS is reversible, making it a potential therapeutic target. Clinical trials using IgY supplements in MS are limited but have shown positive outcomes, including reduced symptoms, and altered immune responses. Combining IgY therapy with other interventions in MS and investigating correlations between microbiota changes and clinical outcomes should be further studied.

Conflicts of interest: None to declare.

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